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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/561,101

05/26/2006

Brian Smith

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EXAMINER

LEESER, ERICH A

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

06/20/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/561,101	<b>Applicant(s)</b> SMITH ET AL.	
	<b>Examiner</b> Erich A. Leeser	<b>Art Unit</b> 1624	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 March 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-3,9,11,12,17,19-37,39,45,46,48,49,51,52,54,59 and 79-83 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3,9,11,12,17,19-37,39,45,46,48,49,51,52,54,59 and 79-83 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1-18-08 and 3-26-08</u> .                                     | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

This action is in response to Applicant's Amendment and Reply to Office Action dated March 26, 2008 in which Applicant amended claims 1, 36, 45 and adding claims 81-83. Claims 1-3, 9, 11-12, 17, 19-37, 39, 45-46, 48-49, 51-52, 54, 59 and 79-83 are currently pending and under examination.

#### ***Information Disclosure Statement***

The references disclosed in the IDS documents dated January 18, 2008 and March 26, 2008 are made of record.

#### ***Claim Rejections – 35 U.S.C. § 112***

Examiner previously rejected claims 1-3, 9, 11-12, 17, 19-37, 39, 45-46, 48-49, 51-52, 54, 59 and 79-80 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for making solvates of the claimed invention.

Applicant argues that West is “entirely irrelevant to the question of enablement of the presently claimed invention” because it deals with “*inorganic atomic solids*.”

As such, Applicant’s own reference clearly teaches that making solvates from organic compounds is not "merely routine" and is very unpredictable: "Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is *complex and difficult*. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and

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features favor the formation of crystals without solvent; these compounds tend to be stabilized by efficient packing of molecules in the crystal lattice, whereas other crystal forms are more stable in the presence of water and/or solvents. There may be too many possibilities so that *no computer programs are currently available for predicting the crystal structures of hydrates and solvates.*" (Emphasis added). Vipagunta et al., *Crystalline Solids*, Advanced Drug Delivery Reviews 48 (2001) 3-26.

The scope of "solvate" is not adequately enabled or defined. Applicants provide no guidance as how the compounds are made more active *in vivo*. Solvates cannot be predicted and there fore are not capable of being claimed if the Applicant cannot properly enable a particular solvate.

Because Examiner finds Applicant's argument unpersuasive, this rejection is maintained with regards to claims claims 1-3, 9, 11-12, 17, 19-37, 39, 45-46, 48-49, 51-52, 54, 59 and 79-80 and expands it to include new claims 81-83.

Examiner previously rejected claims 33-37, 39, 45-46, 48, -49, 51-52, 54 and 80 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant compounds to modulate or treat a 5HT<sub>2C</sub> receptor associated disorder, treat disorders of the central nervous system, treat damage to the CNS; treat cardiovascular disorders; treat GI disorders; treat diabetes insipidus or sleep apnea; decrease food intake, control weight gain or induce satiety of an individual comprising administering a

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therapeutically-effective amount of a compound of Formula (I) or enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

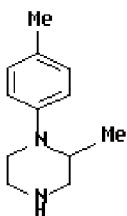
Applicant argues by citing page numbers from the specification that it is Applicant's position that the instant compounds are capable of treating the various stated disorders identified in the rejected claims. However, Applicant admits that "further experimentation such as obtaining clinical data might be required before a given compound would be able to be sold as a drug for the treatment of any particular disease" clearly shows an acknowledgement on the part of the Applicant that the enablement requirement has not been met. As such, Examiner maintains this rejection with regards to 33-37, 39, 45-46, 48, -49, 51-52, 54 and 80 and expands it to include new claims 81-83.

***Claim Rejections 35 U.S.C. § 103***

Examiner previously rejected claims 1-2, 11-12, 17, 19-26, 32 and 79 under 35 U.S.C. § 103(a) as being unpatentable over Allen, et al., U.S. Patent No. 3,751,417.

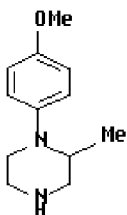
Applicant argues that the proviso of claim 1 excludes the compound:

2-methyl-1-(4-methylphenyl)-piperazine with the following structure.



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Examiner disagrees. In fact, claim 79 exactly teaches this compound. Examiner does agree, however, that the proviso excludes the compound 1-(4-methoxyphenyl)-2-methyl-piperazine with the following structure

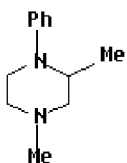


from claim 1. However, the proviso does not exclude the ethyl or ethoxy versions of this exemplified compound, or positional isomers. As such, Examiner maintains this rejection with regards to claims 1-2, 11-12, 17, 19-26, and 79, but withdraws it with regards to claim 32 because the reference does not teach or suggest pharmaceutical compositions.

Thus, it would have been obvious to one having ordinary skill in the art at the time that the invention was made to make similar compounds of Allen, et al.

Examiner previously rejected claims 1, 3, 11, 12, 17, 19-25 and 79 under 35 U.S.C. § 103(a) as being unpatentable over Kametani, et al., *Studies on the Syntheses of Heterocyclic Compounds. CDLX. Benzyne Reaction. XIII. Benzyne Reaction of Halogenobenzenes with N-Alkylmorpholines*, J. Org. Chem., Vol. 37, No. 9, 1450-1453 (1972).

Although the proviso of claim 1 does in fact exclude the compound 2,4-dimethyl-1-phenyl-piperazine with the following structure



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from claim 1, the proviso does not exclude the ethyl version of this exemplified compound, or positional isomers. As such, Examiner maintains this rejection of claims 1, 3, 11, 12, 17, 19-25 and 79.

Thus, it would have been obvious to one having ordinary skill in the art at the time that the invention was made to make similar compounds of Kametani, et al.

### ***Claim Rejections - 35 USC § 102***

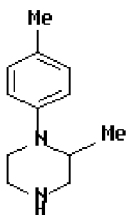
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 11-12, 17, 19-26, 32 and 79 are rejected under 35 U.S.C. § 102(b) as being unpatentable over Allen, et al., U.S. Patent No. 3,751,417.

2-methyl-1-(4-methylphenyl)-piperazine with the following structure.



anticipates the aforementioned claims when R<sup>2</sup> and R<sup>5</sup> are C<sub>1</sub> alkyl, and R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>6</sup> are all H.

Allen, et al. teaches piperazine compounds useful for treating pain, which include instant compounds. Therefore, the instant claims 1-2, 11-12, 17, 19-26, 32 and 79 are anticipated by Allen, et al., U.S. Patent No. 3,751,417.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Erich A. Leeser whose telephone number is 571-272-9932. The Examiner can normally be reached Monday through Friday from 8:30 to 6:00 EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) toll-free at 866-217-9197. If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Erich A. Leeser/

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